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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,432	10/27/2003	Kathleen C.M. Campbell	SIU 7399	8934

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SENNIGER POWERS
ONE METROPOLITAN SQUARE
16TH FLOOR
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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	03/28/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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uspatents@senniger.com

Office Action Summary	Application No.	Applicant(s)	
	10/694,432	CAMPBELL, KATHLEEN C.M.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-13,15-25 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-13,15-25, 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9, 11-13, 15-25 and 27-29 are presented for examination.

Applicant's Amendment filed December 22, 2006 has been received and entered into the present application.

Claims 1-9, 11-13, 15-25 and 27-29 are pending and under examination. Claims 14 and 26 are cancelled and claims 1, 11, 15-17, 19, 22 and 24-25 are amended.

Applicant's amendments to the claims and arguments, filed December 22, 2006, have been fully considered. Accordingly, the reference to Mathur et al. as applied under 35 U.S.C. 103(a) has been hereby withdrawn. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3, 5-9 and 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claims 2-3, 5-9 and 23-24 are each directed to a method for treating alopecia in a patient exposed to radiation for a time and intensity sufficient to result in alopecia comprising orally or parenterally administering to said patient an effective amount of a protective agent comprising methionine or a pharmaceutically acceptable salt thereof, wherein the methionine is administered prior to, simultaneously with, or both prior and subsequently to radiation exposure.

In particular, it is unclear how the subject matter of present claims 2-3, 5-9 and 23-24 are intended to further limit the parent claims from which they depend because each claim involves either administration prior to or simultaneously with the radiation exposure. However, the parent claims from which these claims depend each specifically require that the patient to whom the protective agent is to be administered has already previously been exposed to the radiation prior to the administration of the methionine compound. In other words, it would be impossible to administer the claimed protective methionine agent prior to the patient's exposure to the radiation that induces the alopecia if the patient must already have been exposed to the radiation to induce the alopecia in order for them to be treated according to the presently claimed method.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and, therefore, do not reasonably apprise one of ordinary skill in the art at the time of the invention of metes and bounds of the claimed invention.

For the purposes of examination, claims 2-3, 5-9 and 23-24 will not be further considered herein because they are directed to an administration scenario that is impossible to execute.

Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 11-13, 15-22, 25 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dye (U.S. Patent No. 5,122,369; 1992) in view of Jacobs et al. ("Treatment of Radiation-Induced Alopecia", *Head Neck Surg*, 1979; 2(2):154-159, Abstract Only).

Present claims 2-3, 5-9 and 23-24 are not included in the present rejection because they fail to further limit the subject matter of the parent claim from which they depend for the reasons described *supra* and also because they are directed to an administration scenario that is not possible to execute (i.e., because it would be impossible to administer the protective agent prior to radiation exposure if the patient of the independent claim must have already been exposed to the radiation to induce the alopecia).

Dye teaches a nutrient composition for decreasing the rate of hair loss via the daily consumption of an orally acceptable composition (col.2, l.44-52) comprising d,l-methionine, pantothenic acid and divalent iron in an amount sufficient to effect reduction of the rate of hair loss (col.2, l.65-68). Dye further teaches that d,l-methionine is present in an amount sufficient to effect reduction of the rate of hair loss (col.2, l.47-52).

The teaching of racemic d,l-methionine meets Applicant's limitations of present claims 11 –13 or 22, which provide for the use of d-methionine or l-methionine, since by the very nature of racemic methionine, both the d- isomer and the l- isomer are present.

Regarding the use of the composition of Dye for the treatment of alopecia in a patient that had been exposed to radiation for a time and intensity sufficient to result in the alopecia, Jacobs et al. provides teachings that radiation alopecia is a well-known complication in patients undergoing high-dosage radiotherapy (abstract). In view of such a teaching, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the composition of Dye for treating radiation-induced alopecia because Dye specifically teaches that the composition is effective to reduce the rate of hair loss. Accordingly, one of skill in the art would have reasonably expected success in treating radiation-induced alopecia because the efficacy of methionine in reducing the rate of hair loss would have naturally ameliorated radiation-induced alopecia by decreasing the amount of hair actually lost and slowing the progression of the alopecia, absent factual evidence to the contrary.

Regarding the presently claimed dosage regimens or schedule of administration (claims 4, 15-18, 20-22, 25 and 28-29), the determination of the optimum dosage regimen and schedule of administration to treat alopecia with the presently claimed active agent would have been a matter well within the purview of one of ordinary skill in the art. Such a determination would have been made in accordance with a variety of factors, such as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage regimen and schedule of administration that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific dosage amounts and schedule of administration are not seen to be inconsistent with that which would have been determined by, and well within the routine skill of, the skilled artisan.

In addition, the concentration of the active ingredient is a result-effective variable, i.e., a variable that achieves a recognized result, and, therefore, the determination of the optimum of workable dosage range would be well within the practice of routine experimentation by the skilled artisan, absent factual evidence to the contrary, and, further, absent any evidence demonstrating a patentable difference between the compositions used and the criticality of the amount(s).

As taught by the MPEP at §2144.05, "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Additionally, it is noted that the supplemental administration of the active composition following the administration of an effective amount of the composition would have been *prima facie* obvious to one of ordinary skill in the art motivated by the desire to prolong the therapeutic benefit of the composition to the patient receiving the composition and to also maximize the therapeutic efficacy of the composition in treating the patient's alopecia.

Double Patenting

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Provisional Rejection (New Grounds of Rejection)

Claims 1-9, 11-13, 15-25 and 27-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 17 of U.S. Patent Application No. 11/539,975 in view of The Merck Index (Eleventh Edition, 1989; Monograph 5896, Page 943).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claim is either anticipated by, or would have been obvious over, the reference claims.

Although the conflicting claims are not identical, the claims of the instant application and those of the '975 application are not considered to be patentably distinct from each other because the present claims clearly render the copending claim obvious.

The present claims clearly provide for the administration of methionine (corresponds to the copending compound defined by the formula 1, wherein m=0, n=2, Y=-NR1R2, R1 and R2=H and X=-COOH, which is considered to inclusive of d-, l-, or dl-isomers; see The Merck Index for the known chemical structure of methionine) to a patient exposed to radiation for a time and at an intensity sufficient to result in alopecia.

Though the present claims are directed towards specific dosage regimens and schedules of administration of the claimed methionine agent, the determination of the optimum dosage regimen and schedule of administration to treat alopecia with the presently claimed active agent would have been a matter well within the purview of one of ordinary skill in the art. Such a determination would have been made in accordance with a variety of factors, such as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage regimen and schedule of administration that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific dosage amounts and schedule of administration are not seen to be inconsistent with that which would have been determined by, and well within the routine skill of, the skilled artisan.

In addition, the concentration of the active ingredient is a result-effective variable, i.e., a variable that achieves a recognized result, and, therefore, the determination of the optimum of workable dosage range would be well within the practice of routine experimentation by the skilled artisan, absent factual evidence to the contrary, and, further, absent any evidence demonstrating a patentable difference between the compositions used and the criticality of the amount(s).

As taught by the MPEP at §2144.05, "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Additionally, it is noted that the supplemental administration of the active composition as recited in the instant claims following the administration of an effective amount of the composition would have been *prima facie* obvious to one of ordinary skill in the art motivated by the desire to prolong the therapeutic benefit of the composition to the patient receiving the composition and to also maximize the therapeutic efficacy of the composition in treating the patient's alopecia.

Accordingly, rejection of claims 1-9, 11-13, 15-25 and 27-29 of the present application is deemed proper over claim 17 of U.S. Patent Application No. 11/539,975 as claiming an obvious and unpatentable variant.

Non-Provisional Rejection

Claims 1-9, 11-13, 15-25 and 27-29 remain rejected under the judicially created doctrine of obviousness-type double patenting over patented claims 35-36 of U.S. Patent No. 6,187,817, already of record, for the reasons of record set forth at pages 12-14 of the previous Office Action dated September 22, 2006, of which said reasons are herein incorporated by reference, and in further view of newly cited Jacobs et al. ("Treatment of Radiation-Induced Alopecia", *Head Neck Surg*, 1979; 2(2):154-159, Abstract Only).

Cancellation of claims 14 and 26 renders the instant rejection moot against such claims.

Applicant traverses the present rejection on the grounds that a person of skill in the art would have known that the mechanisms of cell damage are different for different insults (e.g., platinum coordination compounds versus radiation) and would not have known that a protective agent for toxicities arising from platinum-coordination compounds would necessarily be effective as a protective agent against toxicities arising from radiation.

Applicant's traversal has been fully and carefully considered in its entirety, but fails to be persuasive.

First, it is noted that Applicant alleges on the record that the mechanism of cellular damage that

would occur from a platinum agent is distinct from that which would occur from radiation, but provides no evidence in support of such an assertion. Accordingly, such remarks are no more than allegations without factual support. Please see, e.g., MPEP §716.01(c)[R-2](II), which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965)."

Second, Jacobs et al. provides teachings that that radiation alopecia is a well-known complication in patients undergoing high-dosage radiotherapy (abstract). In view of such a teaching, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to adapt the method for treating alopecia as it would result from CDDP toxicity for use in treating patients with alopecia as it would result from radiation toxicity because the '817 patent expressly teaches the efficacy of the methionine compound for treating hair loss. Accordingly, one of skill in the art would have reasonably expected success in treating radiation-induced alopecia because the efficacy of methionine in treating hair loss would have been expected to have the same or substantially similar efficacy in treating alopecia of any etiology, absent factual evidence to the contrary. Further, Applicant has not demonstrated any difference in the mechanism of alopecia as it would result from platinum compounds versus that which would have resulted from radiation, and, therefore, there is no basis for alleging any difference between the two conditions, since they both result in hair loss.

For these reasons, and those previously made of record at pages 12-14 of the previous Office Action dated September 22, 2006, rejection of claims 1-9, 11-13, 15-25 and 27-29 remains proper and is **maintained**.

Conclusion

The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Please reference Gass et al. ("Effect of Stereoisomers of Sulfur-Containing Amino Acids on Local Skin Protection in X-Irradiated Mice", *Aerospace Medicine*, 1967; 38(7):708-712).

Rejection of claims 1-9, 11-13, 15-25 and 27-29 remains proper and is **maintained**.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leslie A. Royds
Patent Examiner
Art Unit 1614

March 15, 2007

3/17/07
ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER